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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,609	04/30/2006	Hesheng Zhang	TJCZ-00101-NUS	3461
33794	7590	07/14/2009	EXAMINER	
MATTHIAS SCHOLL 14781 MEMORIAL DRIVE SUITE 1319 HOUSTON, TX 77079			CHANG, CELIA C	
			ART UNIT	PAPER NUMBER
			1625	
			NOTIFICATION DATE	DELIVERY MODE
			07/14/2009	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 10/595,609	<b>Applicant(s)</b> ZHANG, HESHENG	
	<b>Examiner</b> Celia Chang	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 April 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 11-22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 11-22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. Applicant's election with traverse of species wherein formula I, R1 is hydrogen, R2 is methoxy, R3 is methoxy, R4 is hydrogen, R5 is phenyl, n is 0 in the reply filed on April 15, 2009 is acknowledged. The traversal is on the grounds that no evidence that searching the complete scope would be burdensome. This is not found persuasive because the reactivity of n is 1-2 compounds (ethyl/propyl compounds) would be so different that a search of the benzyl compounds. Benzyl compound has unique reactivity (see Morrison & Boyd p.397-398) which are not co-extensive with other substituted phenylalkanes. The starting material for R1-R5 would be included in the search.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-6, 11-22 formula I n=0 is prosecuted. The remaining compounds are withdrawn from consideration per 37 CFR 1.142.

2. The claim to priority benefit of CN 200320206920.3 cannot be granted because a certified translation of the priority document has not been submitted to the record. The application date is the PCT application date of April 6, 2006.

3. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential element, such reagents, solvents and conditions etc. therefore rendered the claims with unclear and indefinite conditions of the process. See MPEP § 2172.01. Please note that solvents, temperature, pressure and reagents such as alkylating agent have not been specified as to clearly and definitely claim applicants process. Especially, step (c) the term alkylation is not limited to "N" alkylation and no reagents for forming the particular alkylated product has been pointed out.

4. Claims 1-6, 11-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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Please note that a search of the starting material i.e. formula II or III of the claims indicated that other than those compounds wherein R1-R5 disclosed in CA 110:173102; CQ114:6302 or CA 69:2371, nowhere were the compounds broadly encompassed by formula II or III were found i.e. tetrafluoro, tetramethyl, tetramethoxy, or mix and match of the different substituents etc. Absent of starting material, the specification offered mere language rather than enablement. In re Moersch 104 USPQ 122. In re Howarth 210 USPQ 689. . Please note that the solubility, reactivity and stereo hindrance of such tetra-substituted compounds encompassed by the generic scope are so different from the exemplified one single species of R2 is methoxy, R3 is methoxyl, R5 is phenyl, R1, R4 are hydrogen compound, as to constitute a teaching away from the claimed scope. Especially, only limited members of the generic scope were at the time the invention was made.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 4-6, 11-22 rejected under 35 U.S.C. 102(e) as being anticipated by Reddy et al. US 7,148,354, see col. 3-4 and description of detailed conditions.

Even if applicants perfected the priority benefit, the Reddy et al. reference still antedate. In addition, there would be a 102(g) issue between the Reddy et al. claims and the instant claims.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims s 1-2, 4-6, 11-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lensky US 5,606,064 in view of WO97/22584 (both recited on 1449).

*Determination of the scope and content of the prior art (MPEP §2141.01)*

Lensky '064 disclosed very similar steps for a process of making compound of formula I, see examples 2, 4 and 6 wherein the strong acid is toluensulfonic acid, the catalyst is platinum dioxide with generic optional choices to palladium on carbon see col. 2 lines 16-18).

*Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)*

The difference between the continuous steps in examples 2, 4 and 6 and the instant claims is that instead of alkylation being performed at the last step, it was performed before hydrogenation. WO 97/22584 disclosed analogous process for making the same formula I compound wherein alternative solvents, temperature etc. have been clearly described (see p.18, examples 5-6, co-ppt line 23) and operated in alkylation before hydrogenation.

*Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)*

One having ordinary skill in the art would found the changing of sequence for hydrogenation and alkylation is prima facie obvious, since such sequence of steps are independent for different function groups. Especially, the prior art indicated the non-alkylated product is also desirable thus, suggested such independent sub-steps for operation in stepwise derivatization of independent functional groups. Therefore the prior art provided suggestion that the synthetic process can be optional and in any sequence because they all will give the resulting product. *Cohn v. Comm* 148 USPQ 486.

The limitations in the dependent claims are alternative operating parameters clearly suggested in analogous art i.e. WO 97/22584 and demonstrated to be operable in similar steps are mere picking and choosing of an effect oriented parameter for maximum product yield which is prima facie obvious in the chemical art. *In re Geisler* 43 USPQ 1362. *In re Aller* 105 USPQ 233.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 11-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lensky US 5,606,064 in view of WO97/22584 (both recited on 1449) further in view of Devries et al. US 5,916,902.

*Determination of the scope and content of the prior art (MPEP §2141.01)*

Lensky '064 disclosed very similar steps for a process of making compound of formula I, see examples 2, 4 and 6 wherein the strong acid is toluensulfonic acid, the catalyst is platinum dioxide with generic optional choices to palladium on carbon see col. 2 lines 16-18).

*Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)*

The difference between the continuous steps in examples 2, 4 and 6 and the instant claims is that instead of alkylation being performed at the last step, it was performed before hydrogenation. The broad scope and the scope of the dependent claims 2-3, being that the N-benzilation of the piperidinyl nitrogen is optionally by benzylbromide (claim 2) or benzaldehyde with reduction.

WO 97/22584 disclosed analogous process for making the same formula I compound wherein alternative solvents, temperature etc. have been clearly described (see p.18, examples 5-6, co-ppt line 23) and operated in alkylation before hydrogenation.

Devries et al. '902 suggested that N-benzilation can be carrier out by bezylating agent such as benzyl halide and base or benzaldehyde in the presence of a reducing agent (see abstract and col. 8, lines 13-24, col. 11 lines 13-29).

*Finding of prima facie obviousness---rational and motivation (MPEP§2142-2143)*

One having ordinary skill in the art would found the changing of sequence for hydrogenation and alkylation is prima facie obvious, since such sequence of steps are independent for different function groups. Especially, the prior art indicated the non-alkylated product is also desirable thus, suggested such independent sub-steps for operation in stepwise derivatization of independent functional groups. Therefore the prior art provided suggestion that the synthetic process can be optional and in any sequence because they all will give the resulting product. Cohn v. Comm 148 USPQ 486.

The limitations in the dependent claims are alternative operating parameters clearly suggested in analogous art i.e. WO 97/22584 and demonstrated to be operable in similar steps

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are mere picking and choosing of an effect oriented parameter for maximum product yield which is prima facie obvious in the chemical art. In re Geisler 43 USPQ 1362. In re Aller 105 USPQ 233.

The optional alternative N-alkylation is art recognized equivalencies as optional choices of the N-benzylation of the piperidinyll nitrogen. The inclusion of optional choices conventional to one skilled in the art is prima facie obvious since absent of unexpected result there is nothing unobvious in choosing one or the other alternative equivalency taught by the field and demonstrated to be equally operable in producing the desirable benzylated compounds (see Devries et al. '902, col. 11 example 5, step (b) alternative (i) and (ii)).

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 11-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddy et al. '354 in view of Devries et al. US 5,916,902.

Determination of the scope and content of the prior art (MPEP §2141.01)

Reddy et al. '354 disclosed anticipatory process wherein the N-alkylation was performed with benzylating agent benzylbromide (see col. 3-4 and detailed description)

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claim 3 and the broad scope of claim 1 is that the N-benzylation of the piperidinyll nitrogen is optionally by benzylbromide (claim 2) or benzaldehyde with reduction (claim 3). Devries et al. '902 disclose process for making analogous compounds wherein Devries et al. '902 suggested that N-benzylation can be carrier out by benzylating agent such as benzyl halide and base or benzaldehyde in the presence of a reducing agent (see abstract and col. 8, lines 13-24, col. 11 lines 13-29).

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*Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)*

One having ordinary skill in the art would find that the optional alternative N-alkylation using benzaldehyde instead of benzylbromide is an optional choices of the N-benylation of the piperidiny1 nitrogen using the art recognized equivalency. The inclusion of optional choices conventional to one skilled in the art is prima facie obvious since absent of unexpected result there is nothing unobvious in choosing one or the other alternative equivalencies taught by the field and demonstrated to be equally operable in producing the desirable benzylated compounds (see Devries et al. '902, col. 11 example 5, step (b) alternative (i) and (ii)).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*OACS/Chang*  
*Jun 29, 2009*

*/Celia Chang/*  
*Primary Examiner*  
*Art Unit 1625*